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MUSHROOM POISONING AND ITS CLINICAL MANAGEMENT: AN OVERVIEW

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ABSTRACT

In more development countries incidence and mortality rate risen among population due to mushroom poisoning. Edible mushroom for cooking and medical purpose was practiced from olden days and the risk involved for mistaken identity of poison mushrooms possess toxins which are secondary metabolites produced in specific biochemical pathway. Injection of poisonous mushrooms will lead to organ failure even it causes death. We did a systematic review of the published articles on epidemiology; diagnostics and treatment of mushroom poisoning from various literatures are reviewed. This review results *Amanita* species was frequently occurred poisoning when compare other species. Majority of the fatal poisoning worldwide attributable to amanita phalloides appropriately named as death cap. Our review suggest that most of mushroom poisoning are reported in developed countries whereas, least percentage of mushroom poisoning reported in developing countries**.**

Key words: Amanita species, epidemiology, Galerina Species, and Mushroom poisoning.

INTRODUCTION

Every year all over the world health care facilities such as first aid and poison information centres receive hundreds of thousands of cells related to poisoning or toxic exposure involving human pets and animals. The categories of potential hazardous substances includes house hold cleaning, body care products, plants, Mushrooms, Insecticides chemicals and other materials. Plants and mushrooms are included among the high risk categories owing to their potential toxicity. These are due to the fact that they are difficult to classify and some poisonous species are early mistaken for edibles (Leszek satori *et al*., 2005; Mirca Zotti *et al*., 2001). It refers to deleterious effects from ingestion of toxic substances present in a mushroom. The toxins present are secondary metabolites produced in specific biochemical pathways in the fungal cell. Majority of fatal poisoning worldwide are attributable to the Amanita Phalloides mushroom appropriately named "death cap"; other dangerous species of mushrooms are Amanita verna, Amanita virosa, Gyromitra, Gallerina and Lepiota species all of which contain amatoxin, a potent cytotoxin. Ingestion of even a portion of one mushroom of a dangerous species may be sufficient to cause death. Lethal dose of Amatoxin is 10mg, the amount found in a single death cap mushroom (Patowary, 2010). It is usually the result of ingestion of wild mushrooms due to misidentification of a toxic mushroom as an edible species bearing close resemblance. It is also found as a result of small children, especially toddlers in the 'grazing' stage ingesting mushrooms found in the lawn. "Magic" mushrooms are intentionally taken by adolescents for their hallucinogenic effects (Jones Al *et al*., 2006). The experience of a pool of scientists such as physician, a botanist and mycologist is often needed to correctly identifying the toxicant. For this reason accidental poisoning attributable to mushrooms represents an extremely critical task for doctors working in first aid centres because they must quickly identify the correct toxic agent involved (Mirca Zotti *et al*., 2001).

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SPECIES AND ITS CLINICAL TOXICITIES

From 10,000 species of mushrooms growing all over the world, only about 50-100 are known to be toxic (Aji Dy, 1995). One mushroom (50g) is sufficient to kill an average adult (LD 50) 0.2–0.75 mg/kg body weight (Sabeel AL *et al*., 1995; Hanrahan JP *et al*., 1984).

Mushroom poisoning should be considered in differential diagnosis of any case of acute gastroenteritis, especially during spring and fall when moderate temperature and moist condition facilitate mushroom growth (Rengstorff DS *et al*., 2003). By far the majority of mushroom poisonings are not fatal, but the majority of fatal poisonings are attributable to the Amanita phalloides mushroom (Brian paasso *et al*., 1975). Available data indicate that mushroom poisoning, although mostly accidental, is sometimes deliberate. A majority of Poison Center calls concern suspected ingestions by small children, especially backyard-grazing toddlers. Most adult "poisonees" are amateur collectors consuming mushrooms they pick. The majority of illnesses are self-limited GI reactions and an uncertain but likely high proportion of affected individuals never seek medical attention. Importantly, some reactions are idiosyncratic and involve fungi that are widely consumed and well tolerated by those eating them. Nonetheless, almost all *severe* poisonings involve misidentified wild fungi. Mistakes involving *Agaricus bisporus* (death cap) are particularly likely to be tragic. Some of these pickers may mistake death cap for edible Volvariella spp, such as the paddy straw mushroom, which is used in Southeast Asian cuisines. Poisoning among other immigrant groups, such as those from Eastern Europe or from Mexico or Central America, also occurs as a result of unfamiliarity with US species. Some of the poisoning due to mistaken identity was given in Table 1.

Table 1. Common mistaken identity of poisonous mushrooms

Poisonous fungus	Mistaken for these edible fungi
A phalloides (death cap)	Amantia Ianei (coccoli) or Volvareilla spp (eg. Paddy straw mushroom)
Galerina marginata	Psilocybe spp (magic mushrooms)
A smithiana	Tricholoma magnivelare (matsutake)
A muscaria (fly agaric)	Amantia caesaraialjacksonii
Chlorophyllum molybdities (green spored parasol)	Lepiota rachodes (shaggy parasol)
Omphalotus spp	Cantharellus spp or Laetiporus Spp
Gyromitra esculenta	Morchella spp (morels)

Edible Mushrooms

There are about 200 species of edible mushrooms available. *Agaricus bisporus* is the common edible mushroom. It is grown commercially from spawn, a mass of soil and rotting leaves that contains the mycelium of the fungus. Other species are; *Agaricus campestris, Morchella esculenta* and *Volvaria terastria.*

Poisonous Mushrooms

It is very difficult to distinguish between edible and poisonous mushrooms. On the basis of experience, there are some observations, which may help to identify the poisonous mushrooms: bright color, pink spores, a hot burning taste or acidic flavor, growing on wooden pieces in hidden places, difficult to break and bear a cup like structure (volva) at the base. Some of the poisonous mushrooms when taken orally produce hallucinations. These include toadstools of the genera *Amanita, Psilocybe and* Conocybe (Pinson CW *et al*., 1999).

Fig 1: Amantia muscaria

More than 15 cyclopeptides have been isolated from the genus *Amanita* and the most dangerous ones are amatoxins. The pathophysiology of Amanita phalloides depends on its potent toxins so called “amatoxins”. Although phallotoxins and other group of Amanita phalloides toxins are extremely potent hepatotoxins, they are not well absorbed in gastrointestinal tract and therefore contribute little to Amanita toxicity (Jaeger A *et al*., 1993). Amatoxins are actively absorbed from GI tract, bind very weakly to serum proteins, are excreted through the biliary system and kidneys, are usually detectable in plasma during first 36 hours of ingestion, and however are not present in the urine until day 4 (Jaeger A *et al*., 1993).

General guidance’s for identification of different species and its clinical manifestations

These early symptoms may be due to compounds other than the primary toxin or may represent a biphasic response to the primary toxin in susceptible patients.

Onset of symptoms less than 4 hours after ingestion

1. Nausea, vomiting, diarrhoea, abdominal cramping with no progression beyond GI involvement—GI toxins, irritants and idiosyncrasies. A few GI symptoms are delayed .Drowsiness, ataxia, occasional nausea, obtundation (may alternate with hyperkinetic states), muscle fasciculation, seizures.

2. Nausea, confusion, ataxia, feelings of increased strength or euphoria, muscle fasciculation, sensations of floating or color changes, rarely progressing to coma or seizures as in children. Ibotenic acid in adults. It has been shown in Figure:1 *Amanita muscaria* (*Amanita pantherina* complex).

3. Nausea, vomiting, diarrhoea (usually starting in 1-4 hours); progressing to severe malaise, weakness, sweating, cold extremities, confusion, cardiovascular collapse or coma associated with autoimmune hemolysis and damage to kidney and other major organs.

Table 2. Summary of different types of mushrooms and their principle toxin

SPECIES	TOXIN	ONSET	DISTRIBUTION	SYMPTOMS
Amanita (Sp. phalloides, verna, virosa)	Amanitins Phalloidins	GI- 8 to 14 hours Liver- 1-3 days	Found mostly in wooded areas, frequently during late summer and fall seasons.	Gastrointestinal symptoms occur 6 to 24 hours after ingestion. A transient period of improvement is followed by metabolic disturbances and renal and hepatic impairment. Most fatalities occur within several days.
Galerina (Sp.autumnalis, marginata, venenata)	Amanitin.	Not known	These species are found in the western and mid-western United States on lawns, meadows, and decaying Wood.	Symptoms are similar to those of A. phalloides type poisoning.
Gyromita (Sp. esculenta) Helvella (Sp. esculenta, underwoodii)	Monomethyl hydrazine (Gyromitrin)	4 to 12 hrs	These species (except underwoodii) are not confined to any particular habitat or geographic region	These mushrooms produce symptoms similar to intoxication by amanitin but less severe, appearing 6 to 12 hours or more after ingestion. Symptoms are primarily gastrointestinal. Hemolysis and central nervous system effects are associated with these mushrooms.
Inocybe (Sp. napipes) Clitocybe (Sp. rivulosa, trunicola, cerussata, olearia, dealbata)	Muscarine	0.25 to 2 hrs	Commonly found in wooded areas.	Toxins produce "muscarinic" effects, e.g. salivation, lacrimation, nausea, bronchospasm, abdominal pain, vomiting, diarrhoea, headache and miosis within 15 to 30 minutes after ingestion. Bradycardia, and shock may also occur. Death is infrequent.
Amanita (Sp. muscaria, pantherina, cokeri, crenulata, solitaria)	Isoxazole Derivatives: Muscimol Muscazone Ibotenic Acid Pantherin Tricholomic Acid	0.5 to 2 hrs	Commonly found in wooded areas, especially conifer forests of western United States in spring and fall. These mushrooms are also known as "fly mushroom" or "fly agaric."	They produce symptoms resembling the central nervous system effects of excessive atropine and display anticholinergic and mild hallucinogenic properties. Symptoms occur within 1/4-2 hours after ingestion and frequently resemble alcohol intoxication. Severity and duration of symptoms vary with individual. Muscle spasms can occur after ingestion of large quantities.
Psilocybe (Sp. cubensis, eaerulescens, silvatica) Panaeolus (Sp. Foenisecii)	Psilocybin Psilocine	0.3 to 1 hr	Of the 60 species of *Psilocybe* that occur in the United States, 25 are hallucinogenic.	Psychotropic "LSD-like" manifestations begin about 30 to 60 minutes after ingestion and may continue for several hours. Recovery is spontaneous and usually within a day.
Coprinus (Sp. atramentarius)	Monomethyl -hydrazine	Less than 5 hrs	Commonly found across the Northern Hemisphere, including Europe, North America, and Asia, but has also been found in Australia, and also in South Africa	Disulfiram reaction-like symptoms of flushing, Constituents hydrazine palpitation, hyperventilation and tachycardia occur only if alcohol is consumed in combination with these mushrooms. These effects may take place up to 48 hours between ingestion of mushroom and alcohol and last for a short time. Gastrointestinal symptoms of nausea, vomiting, and diarrhoea have also occurred. The severity of symptoms is greatest after ingestion of raw mushrooms.

There is usually a history of earlier ingestions without symptoms. Autoimmune hemolysis. (*Paxillus involutus*).

4. GI symptoms at 4 hours rarely, usually a more delayed onset. Associated kidney failure. See *Amanita smithiana* below (onset of symptoms after 4 hours from time of ingestion).

5. GI symptoms, usually by 4 hours along with haemolysis in association with the ingestion of raw or poorly cooked mushrooms, especially amanitas. Particularly suspect are "blushers" such as *Amanita novinupta* and those amanitas referred to the European name Figure: 2 *Amanita franchetii* (Boud) Fayod.

6. Euphoria, occasional panic reactions, hallucinations, dilated pupils and rarely nausea to the point of vomiting. Look for seizures, fever in children. Psilocybin. (Figure: 3 *Psilocybe*, other dark spored genera).

7. Sweating, salivation, nausea, teary eyes with dilated pupils, slow heart rate and sometimes diarrhoea and increased urination. Large ingestions may cause pulmonary edema and seizures. Muscarine. (Figure 4 & 5*Clitocybe* & *Inocybe*).

8. Within 5-30 minutes of taking alcohol after ingestion of the offending mushroom, the occurrence of flushing, throbbing in the temples, headache, fast heart rate and occasionally nausea and vomiting. Symptoms may recur after alcohol consumption for up to 3 days, but are less severe over time. Coprine. (Figure: 6 *Coprinus*).

9. Rare onsets at 1-4 hours of malaise, vomiting, headache, dizziness usually occurring after 6 hours (Figure: 7 Gyromitrin).

10. Malaise, GI symptoms, severe headache, generalized aching, flushing, incoordination, muscular weakness, difficulty walking and confusion. One hour after ingestion (2 cases). Poisoning with *Stropharia coronilla.*

Onset of symptoms after 4 hours from time of ingestion

1. Sudden malaise, GI symptoms and often severe headache & dizziness at 2-25 hours after ingestion of "false morels". The latency period, which is most commonly 6-12 hours, has been reported as late as 40 hours. Symptoms may progress to muscle cramps, shock, methemoglobinuria, liver failure, fever and CNS symptoms including convulsions. Hemolysis, hemoglobinuria and kidney failure are uncommon. Gyromitrin (*Gyromitra, Helvella*).

2. Diarrhoea, nausea, vomiting, abdominal cramping, malaise usually at 10-16 hours (rarely 5-36 hours) after ingestion progressing to liver failure and rarely kidney failure with decreased urine, shock, acidosis etc. Amanitin (*Amanita phalloides, Amanita ocreata* etc).

3. Diarrhoea, nausea, vomiting 4-10 hours after ingestion (reports range from 5-9 hours) with elevated blood liver enzymes and rare progression to liver failure associated with a description of yellow brown mushrooms clumped on living trees or dead stumps. Poisoning with *Hypholoma fasciculare*.

4. GI symptoms sometimes at 4-12 hours with much later burning and dryness of the mouth at 2 days to 5 weeks progressing to severe thirst, frequent urination of an increased quantity of dilute urine; later having reduced quantity of urine and kidney failure. *Cortinarius rubellus* Cooke.

5. GI symptoms at 4-12 hours followed by kidney failure. (One case of liver failure) Further characterization of the syndrome and the pathological findings are needed. Collection of white mushrooms including presumed matsutake. *Amanita smithiana* Bas.

6. GI symptoms only, but having latencies as long as 4-14 hours on occasion for example, the vase-shaped *Gomphus floccosus*, *kauffmanii* and *bonarii*. Other species such as those in the *Armillaria mellea* complex and some boletes have also had delayed symptoms in Europe.

Fig 2: Amantia franchetii

Fig 3: Psilocybe Semilanleta

Fig 4: clitocybe species

Fig 5: inocybe species

Fig 6: coprinus Atra mentarius

Fig 7: Gyromitra Infula

Fig 8: Galerina Cinnamomea

Fig 9: Galerina Cinnamomea

DIFFERENT TYPES OF TOXIN AND ITS MANAGEMENT

Amanita Toxins

These are characterized by small non-descript carpophores with yellowish brown spores. They often occur in lawns and grassy areas. Poisoning of amanita toxins is characterized by a long latent period between ingestion and onset of symptoms; asymptomatic latent period lasting up to 24 hours precedes violent diarrhoea and vomiting which may cause death. If the patient survives this initial period, the progressive injury to the liver, kidneys, heart and skeletal muscles continues and death results in 50% of the cases within 2-5 days. The treatment includes removal of the toxic material from the GIT, followed by symptomatic and supportive therapy [11]. No antidote is sufficiently established till date. More than 90% of fatalities associated with toxic mushroom ingestion have been attributed to amatoxin containing species such as Amanita phalloides. Galerina sp. and Lepiota sp. are also included in this classification (Erugayen M *et al*., 2007). The mechanism of toxicity relates to interference with RNA polymerase II, which prevents DNA transcription (Faultstich H, 1980). Gastrointestinal effects such as nausea and vomiting are common, but tend to be delayed until 6-24 hours after ingestion, which is a subtle differentiation from other classifications. A quiescent phase, occurring at 12-36 hours after ingestion, may falsely lead patients and physicians alike to believe that a more benign species has been consumed. However, 2-6 days after ingestion, some patients experience hepatic and renal toxicity that can lead to death. These toxicities are caused primarily by alpha-amanitin, a cyclopeptide that is one of the deadliest naturally occurring compounds. As little as 0.1 mg/kg can be fatal, a dose that is often present in a single mushroom. However, elevation of liver enzymes may begin in the quiescent phase, fulminant hepatic failure with elevated transaminases and bilirubin and coagulopathy are not present until the third stage of poisoning. Transfer to a center capable of performing liver transplantation is mandatory if advanced poisoning with evidence of liver failure is present. Multiple studies have attempted to delineate criteria that would merit transplantation, including two of the following: grade 2 hepatic encephalopathy or higher, prothrombin time of more than twice normal despite therapy, bilirubin level greater than

25 mg/dL, and hypoglycemia requiring infusion therapy. Benzathine penicillin is one of the most commonly used therapeutic options but demonstrates little efficacy [19]. The most impressive use of silymarin is in the treatment of *Amanita phalloides* mushroom poisoning, which is an extract from the milk thistle plant (Silybum, 1999). Silymarin's hepatoprotective effects are accomplished via several mechanisms including antioxidation, inhibition of lipid peroxidation (Bosisio E *et al*., 1992; Baer-Dubowska W *et al*., 1998), enhanced liver detoxification via inhibition of Phase I detoxification and enhanced glucuronidation (Halim AB *et al*., 1997; Campos R *et al*., 1989) and protection of glutathione depletion (Fiebrich F *et al*., 1979). Studies have also shown silymarin exhibits several anti-inflammatory effects, including inhibition of leukotriene and prostaglandin synthesis, Kupffer cell inhibition, mast cell stabilization, and inhibition of neutrophil migration (Dehmlow C *et al*., 1996; Fantozzi R *et al*., 1986; Dehmlow C *et al*., 1996; De La Puerta R *et al*., 1996). In addition to these, there are some anecdotal reports about usefulness of hyperbaric oxygen, cimetidine, ascorbic acid, cephalosporines, corticosteroids, cytochrome C, bile salts, heavy metal salts, D-penicillamine and diethyl dithiocarbamate without any confirmed clinical data. Charcoal haemoperfusion, haemodialysis and plasma exchange, although may be theoretically useful but usually they are not practical, because of late presentation in most patients. Thioacetic acid that probably acts as an anti-inflammatory agent and silibinin or silymarine by inhibiting hepatocytes amatoxin uptake, although have been shown to be effective in animals but no convincing data is available for their efficacy in human (Mojtaba varshochi *et al*., 2007).

Pathological features

It reflects the attack of *amatoxin*s on numerous tissues, principally by inhibiting RNA polymerase II in cell nuclei (Faultstich H, 1980). In addition to the liver, pathologic findings may also include small haemorrhages in the tissues and cloudy swelling in the cells of the pancreas, adrenal glands, kidneys, heart, lungs, muscles, intestines and brain. Cardiac muscle occasionally shows fatty degeneration in addition to cloudy swelling. Whereas, central cells of the liver lobules regularly show fatty degeneration and destruction. Changes in the kidney glomeruli (the primary blood filter) may show mild enlargement. In most cases kidneys often display cloudy swelling and destruction in the convoluted tubules near each glomerulus (Constantine D *et al*., 1978).

Post-mortem examination

Amantia virosa poisoning was in the liver, kidneys and brain. The liver had a mottled granular surface. Microscopically there was severe centrilobular liver-cell necrosis with early post-necrotic cirrhosis. Bile stasis was evident in bile ducts and canaliculi, with pseudoduct formation by parenchymal cells about bile lakes in areas of liver cell regeneration and associated with a mild chronic inflammatory reaction. However, renal tubules were dilated and contained bile casts. Calcium deposits were found sprinkled through the renal parenchyma, and there was a mild and diffuse lymphocytic infiltration. In the central nervous system, foci of acute demyelinization were found in the cervical spinal cord, midbrain and cerebral hemispheres, associated with reactive astroglial changes. There were also many areas of perivenous lymphocytic cuffing and demyelination (John lough *et al*., 1970).

Gyromitrin

Helvella esculenta (Gyromitra esculenta Fries), *Helvella gigas* Krombholz are some of the species representing this class. This genus is characterized by pileus surface (nearly smooth to strongly convoluted). Also known as the false morel, appropriately dubbed for its resemblance to the highly prized morel mushroom (Morchella esculenta), the toxic principle is N-methyl-N-formylhydrazone of acetaldehyde. Gyromitra species rarely can cause severe neurologic toxicity and seizures. It is characterized by its toxic effect on liver. While, hematopoietic and the central nervous system is also affected. A minimum latent period of 6-10 hours is observed between onset of symptoms and ingestion of the drug. The treatment is similar to that given in poisoning caused by *Amanita* toxins. Mortality rate ranges between 2-4%. GI symptoms are usually delayed at least 5-10 hours after ingestion, and most patients recover fully. However, because of metabolism, gyromitrin is converted *in vitro* to monomethylhydrazine, which interrupts pyridoxal-phosphate related reactions, including those involved in GABA synthesis. As GABA is an inhibitory neurotransmitter, seizures may be precipitated and can be refractory to benzodiazepine therapy. As in isoniazid overdose, which works biochemically in the same fashion, treatment should include repeated bolus of vitamin B6 (recommended dose of 70 mg/kg IV). Patients with this ingestion should be admitted for neurologic checks.

Orellanine

This genus is characterized by brownish to reddish brown spores. In the large genus *Cortinarius*, which contains more than three hundred species, there are at least two known poisonous species: *Cortinarius orellanus* and *Cortinarius speciosissimus*. Orellanine poisoning is characterized by an extremely long latent period (3-14 days). An intense burning thirst is followed by GIT disturbances, headache, pain in the limbs, spasms and loss of consciousness. Severe poisoning may lead to kidney damage and death after several weeks. About 15% of the cases have proved fatal. With a particularly insidious course, delayed toxicity in this mushroom ingestion may not be preventable. The earliest symptoms, such as gastritis, chills, and headache, tend to occur 1 day after ingestion, but oliguric renal failure tends to begin days to weeks after ingestion. It follows a pattern of interstitial nephritis, and there is no benefit to detoxification by hemodialysis early on; but it is the mainstay of treatment once nephrotoxic damage has set in. Renal transplantation has been warranted in some cases. Symptomatic and supportive treatment with specific maintenance of kidney function is recommended.

Clinical findings

A renal biopsy performed 14 days after ingestion showed interstitial edema, interstitial nephritis, and tubular

necrosis. These laboratory and histopathological abnormalities are consistent with the primary biological features of the renal phase of *Cortinarius* species poisoning (Bryan S *et al*., 2010).

Muscarine

Muscarine is the toxic principle and species of genus *Amanita muscaria* (Fries) Hooker and *A. pantherina* (Fries) represents this class. Muscarine is also found in species of *Boletus, Clitocybe, Lepiota, Hebeloma, Inocybe* and *Russula. Clitocybe* and *Inocybe* contain high concentration of muscarine (3% of dry weight). *Clitocybe* is recognized by white spores, fleshy central stripes, broadly adnate to decurrent gills. *Inocybe* is recognized by its sub-conic to campanulate pileus and brownish spores. Muscarine poisoning can Cause mild cholinergic excess. Serious toxicity is rare due to limited accessibility to mushrooms, poor bioavailability, and small/malodorous nature of the mushrooms. Symptoms develop rapidly, within 2 hours, but may persist for hours more as well. Muscarine poisoning is characterised by increased salivation, perspiration and lacrimation within 15-30 minutes. These symptoms are followed by abdominal pain, severe nausea and diarrhoea. Though the patient's mental condition is stable, pulse rate is slowed down, heavy breathing and the pupil is constricted. The cardiac and respiratory failure leads to death, which is rare. Treatment involves gastric lavage and administration of a specific antidote atropine. Symptomatically controlled patients are safe for discharge.

Ibotenic acid-Muscimol

Common name of *A. muscaria* is the "fly agaric" which contains ibotenic acid and its metabolite, muscimol, which act *in vivo* like glutamic acid and GABA, respectively. Onset of symptoms is typically rapid, within 2 hours, and may produce hallucinations, dysphoria, and delirium. Symptoms last from 4 hours up to 24 hours with severe ingestion. The poisoning is characterized by an initial state of excitement, followed by muscular twitching, depression and loss of consciousness within 1-2 hours. Whereas, in children, symptoms may include seizures and myoclonus. Death is rare and treatment involves mild depressants followed by stimulants and the recovery is rapid. Treatment is supportive, there are no delayed ill effects, and symptomatically controlled patients may be discharged.

Psilocybin

The toxic principle is 2 tryptamine derivatives, Psilocybin and Psilocin. Species of *Psilocybe* and *Conocybe* represents this class. The genus is characterized by the presence of bluish stains near the base of stipe, when the tissue is damaged or becomes aged. Psilocybin poisoning develops rapidly and leads to anxiety and difficulty in concentration and comprehension. It lasts for several hours and true hallucinations may be experienced. Recovery is spontaneous and complete after 5-10 hours. While psilocybin has some similarities to lysergic acid diethylamide (LSD), severe effects such as coma, malignant hyperthermia, and death have been documented only once in mushroom ingestion. In addition to that effects are very rapid, and often only reassurance is needed. However, benzodiazepines also may offer some relief. Discharge is appropriate once vital signs normalize.

Coprine

The last specific rapid-acting toxin, coprine, is found in many Coprinus species. Toxic principles are the constituents resembling disulfiram like or cyanamide. (Figure: 6 *Coprinus atramentarius* (Fries) and the subsequent ingestion of alcohol represent this class. This species is recognized by black spores, smooth or minutely scaly greyish pileus and free gills that deliquesce into a dark colored fluid as the spores are discharged. The mushrooms are also known as "inky caps" because of the substance they produce when picked. Ingested alone, little effect is noted, but subsequent ingestion of alcohol produces a disulfiram-like reaction, with intense vomiting, tachycardia, and flushing. This is caused by inhibition of acetaldehyde dehydrogenase. Poisoning symptoms include: flushing, palpitations, dyspnoea, hyperventilation and tachycardia. Treatment Care, once again, is symptomatic, and vomiting tends to resolve in a matter of hours.

Gastrointestinal Toxic Mushrooms

The majority of mushroom ingestions that present to health care facilities do cause some gastrointestinal (GI) upset. Multiple species are responsible for this phenomenon, and onset of nausea, vomiting, and abdominal pain rapidly follows ingestion, usually in less than 3 hours.

Patients may divulge a history of foraging for edible brown mushrooms, or may admit to searching for hallucinogenic mushrooms. Care is symptomatic, and some patients may present fairly dehydrated. Disposition is similar to that in other causes of gastroenteritis

Management of poisoning

This guideline is intended to be only the basic set of instructions to manage cases of unknown mushroom ingestion, and is by no mean exclusive. There may be exceptions to the guidelines contained, and the user should refer to the individual practice guidelines, other treatment guides, or more detailed literature for specific management of poisoning cases due to mushrooms which have been identified. Specific antidotal therapy is available for very few intoxications by fungi, therefore mainstays of treating poisoning are: decontamination symptomatic and/or supportive therapy, clinical observation and good nursing care.

General approach to the poisoned patient

1. Stabilization and complete patient evaluation

Apply general clinical measures to prevent further deterioration of the patient. Fortunately, poisoning by fungi is NOT a frequent life-threatening situation, but if airway, breathing or circulations are compromised, performs appropriate resuscitative measures. The primary survey of the patient should be carried out simultaneously with resuscitation in case of life-threatening poisoning. After stabilization of the vital signs, an accurate history helps guide further management.

Routine questions should include:

1. What fungus/fungi did you intend to collect
2. What type of tree was it growing near

3. Was it growing in the woods or in the field or the garden
4. On what substrate was the fungus growing
5. Did the fungus have an odor, what was the size and colour, were there gills or "sponge"
6. How many species of fungi were consumed
7. How many persons ate the fungus
8. Was the fungus eaten at more than one meal (what were the exact times of ingestion)
9. How long after exposure did the symptoms begin to appear
10. How was the fungus prepared (raw vs. Cooked)
11. How were the fungi stored between collection and the time of preparation
12. How were the already prepared fungi stored before Ingestion
13. Was any alcohol consumed with the meal
14. Are all people ill who consumed the fungus
15. Are there other ill persons in the group who did not consume the fungi
16. Did the patient ever eat this fungus before
17. Were the mushrooms bought, and if so, where.

If the mushrooms are available and the diagnosis is still unclear, try to have them analyzed by a mycologist, but start treatment without delay if serious poisoning is suspected. In some places the "newspaper" test (the newspaper must contain lignin) is being used: press the mushroom on the newspaper, let it dry and add one drop of hydrochloric acid. The paper may turn to a blue or bluish-green colour indicating the presence of amatoxins. The test is not 100% conclusive.

2. Fungus identification

Accurate identification of the fungus involved (genus and species) helps guide appropriate treatment. In managing the patient poisoned by a fungus, it is mainly more important what the fungus is not, rather than what it is. There are only a few fungal species in which the toxin (e.g. Amantidin, orellanine, gyromitrin) is of such a magnitude that the treatment of the patient must be more than only symptomatic in nature. If available, a trained mycologist should be consulted to help eliminate from consideration the more toxic fungal species.

3. Reduction of absorption

The mainstay in the reduction of absorption is the administration of activated charcoal. Since it only takes a few minutes to adsorb toxins, it should be administered even before gastric lavage or emesis is induced (dosage: 50 to 100 g in adults, 10 to 25 g in children). In general emesis or lavage only removes about one-third of ingested material, so sufficient activated charcoal administration should prove more effective. If microscopic analysis of gastric contents is to be performed, do the sampling, if possible, before administration of a charcoal.

4. Enhancement of elimination

Dialysis and haemoperfusion may be indicated only in very few fungal intoxications (e.g. by cyclopeptides, orellanine), but to be effective it must be undertaken on an early stage of poisoning.

5. Specific fungal antidotes

Few antidotes are available for fungal intoxications. Many propose antidotes have NOT been proven to be useful in controlled clinical studies, but still have their international proponents.

6. Main fungal syndromes and their treatment

Symptomatic treatment of the patient should begin before identification of the fungus in question. Knowledge of certain syndromes characteristic of fungal poisoning is important. Always keep in mind that there can be many causes of symptoms which are NOT directly related to an exogenous fungal toxin: panic reactions (fear of having ingested a highly poisonous fungus), difficulties to digest the fungi, bacterial contamination (Salmonella, Staphylococcus, in the worst botulism), raw fungi (many edible species give arise to gastrointestinal symptoms if not prepared properly), individualized allergic reactions or, rarely, pesticide residues.

It must be remembered that when dealing with fungal toxins, that the longer the time interval (usually > 6 to 12 hours) between ingestion and the onset of symptoms, the more severe the type of fungal toxin (e.g. amatoxin, orellanine, gyromitrin). Long onset indicates the possibility of a severe poisoning.

7. Continuing care

After diagnosis and initial treatment, an adequate observation period should be established, especially if the poisoning is severe. Psychiatric evaluation and counselling is indicated in the case of intentional poisoning (e.g. suicide, substance abuse). Education is recommended in cases of accidental poisoning by fungi, in order to prevent further poisoning incidents. Prevention and educational material is available in a number of poisons centres.

Risk Assessment Recommendations

Accidental Paediatric Ingestion

History

Usually less than 4 years old. Usually a small “nibble” ingestion.

Important historical indicator is that the patient was NOT fed the mushrooms.

Onset of symptoms: No vomiting - Low to no risk

Vomiting within 6 hours of ingestion – Low risk

Vomiting starts after 6 hours – Higher risk

Recommendation.

The majority of these patients can simply be discharged safely from the emergency department. If the patient developed delayed GI symptoms (>6 hours after ingestion), then may want to consider checking AST/ALT and mushroom identification.

Non-accidental-Adult Ingestion

History

Mushroom foragers or fed wild mushrooms that may carry risk.

These need to be taken more seriously.

Late onset of GI symptoms (>6 hours) should raise concern for higher risk.

Recommendation

Asymptomatic:

1) Consider dose of drug given to patient.

2) Check baseline liver enzymes.

3) Recheck liver enzymes in 12-24 hours – This can be done as an outpatient. Instruct patient to return if any symptoms (including vomiting, abdominal pain).
4) Consider sending digital photos of mushroom for mycologist identification.
Symptomatic:
1) IV fluids and anti-emetic medication.
2) Consider dose of Drug.
3) Check baseline liver enzymes.
4) Consider sending digital photos of mushroom for mycologist identification.
5) Serial liver enzyme check at 12 hours. If these remain normal and patient symptomatically better, then can to discharge patients with instructions to return if more/worsening symptoms.
6) Recheck liver enzymes again in 24 hours.
7) If liver enzymes are elevated at any time, then ingestion should be treated aggressively as hepatotoxic mushroom poisoning.
Treatment of Hepatotoxicity (Elevated AST and/or ALT):
1) Aggressive fluid hydration: Patients with early renal failure tend to do worse. Want to maximize toxin excretion with good urine output. Give normal saline boluses then D5 ½ NS at 200 mL/hr.
2) Silibinin (Legalon): Probably the best treatment studied to date. Experimental protocol can be used to give silibinin in Northern California. In cases of significant toxicity (liver enzyme elevations), Silibinin therapy should be instituted as soon as possible.
3) MDAC: Use for GI decontamination early and may help decrease entero-hepatic recirculation later. The primary problem here is that patients are unlikely to tolerate it as they have severe GI upset already.
4) No definite proven benefit in mushroom toxicity but seems to improve survival in all comers with hepatic toxicity. It is very unlikely to result in any harm.
5) Naso-biliary drainage: This is a controversial therapy. Based on animal studies and a single human case report. The drained bile in that report contained very high levels of amatoxin. It is unlikely that we will be able to convince a gastroenterologist to perform. Risks are similar to doing an ERCP.
6) High dose penicillin: No definite proven benefit in mushroom poisoning but unlikely to result in harm. Some have raised concerns that penicillin may decrease the effectiveness of silibinin.
7) Transfer to Liver Transplant Center: Any patient developing evidence of hepatic failure who may be a transplant candidate should be considered for transfer to a centre capable of hepatic transplantation.

CONCLUSION

Our review suggest that most of mushroom poisoning are reported in developed countries whereas, least percentage of mushroom poisoning reported in developing countries, hence in future clinician, researcher should report the clinical toxicities of different species and develop database for management of mushroom poisoning in poor countries. In addition to that, every hospital should have specialised centre to manage and counsel the poisoned patient. Various education programmes should be conducted so that mushroom pickers will recognise the poisonous mushrooms by doing effectively.

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